REMARKS

This response addresses the issues raised by the Examiner in the Office Action mailed June 23, 2008.

Applicant would like to thank the Examiner and the Supervisory Patent Examiner for taking the time to meet with the Applicant and attorney on November 3, 2008. Applicant agrees with the Substance of Interview described in the Interview Summary prepared by the Examiner.

Reply to 35 U.S.C. § 103 Rejection

The Examiner rejected currently pending claims 40-43, 45-69, 71-82, 119-125 and 129-138 in light of Hudis et al. '99 combined with Henderson et al. and Winer et al., under 35 U.S.C. § 103(a). Applicant respectfully requests that the Examiner reconsider his rejection under § 103(a) for the following reasons.

Hudis et al. '99 discloses a sequential and dose-dense treatment regimen using escalated doses for treatment of breast cancer consisting of 3 cycles of doxorubicin 90 mg/m^2, followed by 3 cycles of paclitaxel 250 mg/m^2, and finally 3 cycles of cyclophosphamide 3 g/m^2. (Page 93, abstract.)

Winer et al. discloses the results of CALGB 9342, a non-dose-dense randomized trial of three doses of paclitaxel—175 mg/m^2, 210 mg/m^2 and 250 mg/m^2—in patients with metastatic breast cancer. Winer et al. discloses that "[i]n a proportional hazards model, higher paclitaxel dose" is a "significant predictor[] of longer time to disease progression." Winer et al. further notes that "[d]espite the greater toxicity, formal quality-of-life analysis reveals no difference in patient-related quality of life across the three arms." Finally, Winer et al. notes that "[a]lthough there is a longer time to progression with higher doses, this potential advantage must be considered carefully in light of greater toxicity seen with increasing dose."

According to the M.P.E.P., "it is improper to combine references where the references teach away from their combination." (*See* Section 2145, citing *In re Grasselli*,

713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983).) Hudis et al. '99 expressly teaches away from the low dose paclitaxel disclosed in Winer et al. and the instant specification.

Specifically, Hudis et al. '99 states that "for advanced disease, there seems to be an advantage for 175 mg/m^2 compared with the 135 mg/m^2 when it is administered over 3 hours, *and even higher doses may offer a small additional benefit.*" (Page 98, col. 1, first paragraph.) Accordingly, with respect to paclitaxel, Hudis et al. '99 concludes that "*[w]ith no confirmation that lower doses and 3-hour infusions were equivalent to higher doses* and longer infusions, *and on the basis of the earlier clinical trials of paclitaxel*, we chose to use the latter in this pilot trial." *Id.* In reaching the conclusion that the *higher* dose of paclitaxel should be used, Hudis et al. '99 relied on the same study described in Winer et al.—CALGB 9342—one of "the earlier clinical trials." (*See id.*, fn. 31.)

Thus, Hudis et al. '99 expressly considered the results of CALGB 9342 (i.e., Winer et al.) using the three paclitaxel doses disclosed therein in selecting the appropriate dose for their own study. In light of the results of CALGB 9342, Hudis et al. '99 *rejected* paclitaxel 175 mg/m^2 and instead chose to use the *highest* dose used in CALGB 9342—250 mg/m^2. Clearly, if Hudis et al. '99 did not agree that paclitaxel at 250 mg/m^2 conveyed some treatment advantage, they would not have selected that escalated dose for their own study. There cannot be a clearer example of "teaching away" from the use of 175 mg/m^2 paclitaxel as taught by the instant invention.

For the foregoing reasons, Applicant respectfully submits that currently pending claims 40-43, 45-69, 71-82, 119-125 and 129-138 are unobvious in light of Hudis et al. '99, Henderson et al. and Winer et al. and requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

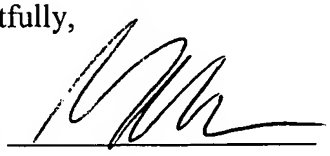
Conclusion

In view of the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this

application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below. If there are any fees due, please charge any such fees to our deposit account No. 501561 and reference attorney docket number 93580.010100.

Respectfully,

Date: December 23, 2008

By: 

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